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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,691	08/29/2000	Gregg B. Fields	110.00680101	3203

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Ann M Mueting
Mueting Raasch & Gebhardt
PO Box 581415
Minneapolis, MN 55458-1415

EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/529,691	FIELDS ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-8,14-21 and 32-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-8,14-21 and 32-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The amendment filed on April 3, 2003 is acknowledged and has been entered. Claims 22-31 have been canceled. Claims 4, 6-8, 14, 16-18, and 32 have been amended. Claims 33-44 have been added.

2. The declaration under 37 CFR § 1.132 by Gregg B. Fields filed on April 3, 2003 is acknowledged and has been entered.

3. Claims 4-8, 14-21 and 32-44 are pending in the application and are currently under prosecution.

Grounds of Objection and Rejection Withdrawn

4. Unless specifically reiterated below, the grounds of objection and rejection set forth in the previous Office action mailed December 3, 2002 have been withdrawn.

Response to Declaration under 37 CFR § 1.132

5. The declaration under 37 CFR § 1.132 by Gregg B. Fields is sufficient to overcome the rejection of claims 4 and 6-8 under 35 USC § 102(b) as being anticipated by Knutson et al. for the reason set forth in section 12 of the Office action mailed December 3, 2002. The declaration states the disclosed D-enantiomer of the peptide designated IV-H1 did not consist of the amino acid sequence set forth as SEQ ID NO: 1, as the peptide comprised an additional C-terminal tyrosine residue. As presently amended, claims 4 and 6-8 are drawn to a polypeptide consisting of the sequence set forth in SEQ ID NO: 1, but which is in the all D-form; therefore, in view of the amendment, the declaration has obviated the rejection.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 6-8, 16-21, and 33-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of a peptide consisting of the amino acid sequence set forth in SEQ ID NO: 1 and optionally conjugated to either a polyethylene glycol molecule or to a C_{10} alkyl molecule to partially inhibit binding of human melanoma cells to type IV collagen *in vitro*, to partially inhibit invasion of MATRIGEL by human melanoma cells *in vitro*, and to partially inhibit formation human melanoma foci in an experimental mouse model of metastasis, wherein the melanoma cells are pre-incubated with the peptide before injection into the mouse, does not reasonably provide enablement for the use of any peptide encompassed by claim 4, 14, or 32 to inhibit the binding, invasion, or metastasis of melanoma cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As set forth in the previous Office action mailed January 2, 2002, the teachings of the specification cannot be extrapolated to the enablement of the claimed invention because in the absence of working exemplification that is commensurate in scope with the claims, one skilled in the art would not be able to use the claimed invention with a reasonable expectation of success without first having to perform an extensive and undue amount of experimentation. Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

One cannot extrapolate the teachings of the specification to the enablement of the invention, particularly in the absence of exemplification that is commensurate in

scope with the claims, because it is well known that the art of drug discovery for is highly unpredictable. With regard to anticancer drug discovery, for example, Gura (*Science* **278**: 1041-1042, 1997) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile (abstract). Gura teaches that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models, but that only 39 have actually been shown to be useful for chemotherapy (page 1041, first and second paragraphs).

Although the teachings of Bergers, et al (*Current Opinion in Genetics and Development* **10**: 120-127, 2000) are drawn to specific antitumor agents, namely matrix metalloproteinase inhibitors, the great extent of unpredictability in the art is underscored by the disclosures of Berger, et al. Bergers, et al teach, "a body of data over the past few years indicate [...] that proteinases and proteinase inhibitors may, under special circumstance, either favor or block tumor progression. For example, ectopic expression of TIMP-1 [a natural inhibitor of metalloproteinases] allows for some tumors to grow, while inhibiting others" (page 125, column 2). In fact, Bergers, et al, disclose that the Bayer Corporation recently halted a clinical trial of a metalloproteinase inhibitor because patients given the drug experienced greater progression of cancer than did patients given a placebo (page 125, column 1). Bergers, et al comments, "these results are somewhat surprising and contrary to Bayers' preclinical data, which confirmed that the drug inhibited tumor activity in rodents" (page 124, columns 1-2). Bergers, et al also teaches that the absence of a metalloproteinase activity in mice actually predisposes the mice to *de novo* squamous carcinomas. Thus, it is relatively clear that one skilled in the art cannot predict the effect of administering a pharmaceutical composition purported to have a desired pharmacological effect to a subject. The efficacy of any unproven drug must be determined empirically and such empirical determinations must be commensurate in scope with its expected and indicated uses.

Additionally, one skilled in the art would not accept the assertion that any polypeptide having an amino acid sequence that is a fragment of the continuous collagenous region of the major triple helical domain of the α1 chain of type IV collagen,

including the peptide of SEQ ID NO: 1, can be used to inhibit the adhesion, invasion, or metastasis of any type of tumor cell based only upon the disclosed examples. In this regard and reminiscent of the teachings of Berger, et al (cited *supra*), it is noted that Nomizu, et al (*Journal of Biological Chemistry* **267**: 14118-14121, 1992) teaches that a peptide derived from laminin, which is a protein also involved in mediating tumor cell adhesion, actually promotes the growth of tumors in a mouse model for studying means for treating human melanoma (abstract). Furthermore, it is duly noted that Knutson et al. (*Proceedings of the American Association for Cancer Research* **36**: 68, Abstract No. 407, 1995) teaches the D-enantiomer of the peptide designated IV-H1, which has the amino acid sequence set forth as SEQ ID NO: 1, did not support migration and has no effect on melanoma cell invasion of a reconstituted basement membrane *in vitro*, whereas the L-form peptide inhibited invasion. In view of the teachings of Knutson et al., the skilled artisan would not expect the peptide of claim 4 to be capable of inhibiting binding of melanoma cells to type IV collagen or inhibiting melanoma cell invasion of a reconstituted basement membrane, and would therefore not accept the assertion that the peptide is capable of inhibiting melanoma metastasis *in vivo*.

One skilled in the art cannot predict the effect of administering a pharmaceutical composition comprising the claimed polypeptide, which is only purported to have a desired pharmacological effect to a subject, and would necessarily have to first perform an extensive and undue amount of experimentation in order to practice the claimed invention with a reasonable expectation of success. Therefore, the disclosure fails to meet the enablement requirement of 35 USC § 112, first paragraph.

Applicant has traversed the grounds of rejection under 35 USC § 112, first paragraph set forth in the previous Office action, arguing the rejection has been rendered moot in view of the amendments to the claims. Applicants' arguments have been carefully considered but have not been found persuasive, as it cannot be understood how the amendment has rendered the rejection moot.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 17, 18, 20, 21, 34, 35, 37, 38, 40, 41, 43, and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17, 18, 20, 21, 34, 35, 37, 38, 40, 41, 43, and 44 are deemed indefinite because claims 17, 18, 34, 35, 40, and 41 recite the term "modulating" to mean "bringing the polypeptide or peptide-conjugate in close proximity to, and preferably so close that it is contact with, the tumor cell", as the term is defined at page 5, lines 11-13. While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). According to The American Heritage® Dictionary of the English Language: Fourth Edition, 2000 the commonly accepted meaning of the term is: "To adjust or adapt to a certain proportion; regulate or temper." Therefore, in the context of the claim, according to the accepted meaning of the term "modulate", the method should comprise the step wherein a discernable or measurable property or attribute of the tumor cell is adjusted, adapted, regulated, or tempered by the polypeptide or polypeptide-conjugate. In view of the unusual meaning, which Applicants have afforded the term "modulating", the claims are indefinite and therefore the metes and bounds of the invention are not properly delineated.

Applicants have traversed this ground of rejection, arguing the claims would be sufficiently clear to the skilled artisan in view of the definition of the term "modulating" at page 5, lines 11-13. Applicants' arguments have been carefully considered but have not been found persuasive.

Amending claims 17, 18, 34, 35, 40, and 41 to recite, for example, "contacting the melanoma tumor cell" with the peptide or conjugate thereof can obviate this ground of rejection.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claim 32 is rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6,096,863 A.

US Patent No. 6,096,863 A teaches a peptide-conjugate comprising a polypeptide having the sequence set forth as SEQ ID NO: 1, which is in the all L-form, wherein the polypeptide is bonded to a non-peptide moiety. The non-peptide moiety of the peptide-conjugate of the prior art is an organic group having a C_6-C_{18} alkyl chain.

12. Claim 32 is rejected under 35 U.S.C. 102(b) as being anticipated by Berndt et al. (*J. Am. Chem. Soc.* **117**: 9515-9522, 1995).

Berndt et al. teaches a peptide-conjugate comprising a polypeptide having the sequence set forth as SEQ ID NO: 1, which is in the all L-form, wherein the polypeptide is bonded to a non-peptide moiety. The non-peptide moiety of the peptide-conjugate of the prior art is an organic group having a C_6-C_{18} alkyl chain.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious

at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 4, 5, 14, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knutson, et al (*Proceedings of the American Association for Cancer Research* **36**: 68, Abstract No. 407, 1995) in view of WO 91/08755 A1.

Knutson et al. teaches the D-enantiomer of a peptide designated "IV-H1", which has the sequence of a fragment consisting of residues 1263-1277 of the α1 chain of type IV collagen. Applicant has provided declaratory evidence that the peptide of Knutson et al. differs from the instantly claimed peptide by a single tyrosyl residue at the terminus.

WO 91/08755 A1 teaches the amino acid sequence of a peptide similarly designated "IV-H1", which is the same as the amino acid sequence instantly claimed. In addition, WO 91/08755 A1 teaches that the peptides can be synthesized with an additional carboxyl-terminal tyrosyl residue, which enables radioactive iodination of the peptide.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to synthesize the D-form peptide of Knutson et al. either with or without the terminal tyrosyl residue, since WO 91/08755 A1 teaches that the sole function of the terminal tyrosyl residue is to enable radioiodination of the peptide. Thus, the inclusion or exclusion of the terminal tyrosyl residue would be recognized as a design choice resulting in equivalent peptides. Therefore, if one were not iodinating the peptide, one would recognize that synthesis of the peptide could be terminated prior to the additional of the tyrosyl residue. If one were iodinating the peptide, the tyrosyl residue would be included and radioiodination of the peptide would result in a peptide conjugated to a cytotoxic and detectable moiety.

15. Claims 32 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knutson, et al (*Proceedings of the American Association for Cancer Research* **36**:

68, Abstract No. 407, 1995) in view of WO 91/08755 A1 as applied to claims 4, 5, 14, and 15 above, and further in view of US Patent No. 6,096,863 A.

Knutson, et al teaches that which is set forth above.

WO 91/08755 A1 that which is set forth above and in addition teaches contacting melanoma cells with L-form peptide inhibits binding of the cells to type IV collagen *in vitro*.

US Patent No. 6,096,863 A ('863) teaches a peptide-conjugate comprising a polypeptide having the sequence set forth as SEQ ID NO: 1, which is in the all L-form, wherein the polypeptide is bonded to a non-peptide moiety. The non-peptide moiety of the peptide-conjugate of the prior art is an organic group having a C_6-C_{18} alkyl chain. '863 teaches the peptide portion of the peptide-conjugate, which has secondary structure, preferably has a biological function, while the lipophilic portion, i.e., the organic group having an alkyl chain of up to 20 carbons, does not detract from the structure of the peptide portion. Moreover, '863 teaches the lipophilic portion may enhance or stabilize the structure of the peptide portion and may facilitate or induce structure formation.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have synthesized a peptide-conjugate comprising a peptide having the sequence set forth as SEQ ID NO: 1, which is in the all L-form, and a non-peptide moiety, which is an organic group having a C_6-C_{18} alkyl chain, as disclosed by '863, and to have used the peptide-conjugate in the manner described by Knutson et al. and WO 91/08755 A1 to inhibit binding of melanoma cells to type IV collagen *in vitro* by contacting the cells with the peptide-conjugate, because '863 teaches the lipophilic or non-peptide portion of the peptide-conjugate does not detract from the structure of the peptide portion. Because the structure of the peptide portion is not affected, the ability of the peptide to inhibit binding of melanoma cells to type IV collagen *in vitro* would not be affected. One of ordinary skill in the art at the time of invention would have been motivated to do so because '863 teaches the lipophilic portion of peptide conjugate may enhance or stabilize the structure of the peptide portion and may facilitate or induce formation of its secondary structure.

16. Claims 4-8, 14, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,013,628-A in view of Dooley, et al (*Science* **266**: 2019-2022, 1994).

US Patent No. 6,013,628-A ('628) teaches a peptide consisting of the amino acid sequence set forth in SEQ ID NO: 1. '628 teaches that the peptide can be conjugated or covalently bonded to a radioisotope, which is a cytotoxic agent. '628 teaches that the polypeptide can be administered to treat a patient diagnosed with a diseases and conditions of the eye, which include scarring and proliferative vitreoretinopathy.

However, '628 does not explicitly teach that the polypeptide can be in an all D-form.

Dooley et al. teaches polypeptides comprised of D-form amino acids are not degraded by proteases and can be expected to remain intact after its administration to a patient and would therefore have a longer half-life following its administration to a pateint.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to have synthesized the polypeptide of '628 in the all D-form, because Dooley et al. teaches that polypeptides in the all D-form are not degraded by proteases after administration to a patient. One of ordinary skill in the art at the time the invention was made would have been motivated to synthesize the all D-form of the polypeptide of '628 because of its long duration of action resulting from its longer half-life following its administration to a patient.

Although neither reference teaches the peptide is capable of inhibiting the binding of melanoma cells to type IV collage, inhibiting melanoma cell invasion into basement membranes, or inhibiting tumor cell metastasis, because the peptide of the prior art cannot be materially or structurally distinguished from the peptide of claim 4, absent a showing of an unobvious difference, the peptide of the prior art is deemed the same as the peptide of the claims 6-8.

Applicant traversed the rejection of claims 4-8, 14, 15, and 32 under 35 USC § 103(a) set forth in section 15 of the previous Office action. Applicant has argued the

prior art does not teach or suggest the claimed polypeptide or conjugate thereof can be used in the claimed methods. In addition, Applicant has argued an absence of proper motivation to combine the teachings of prior art indicates the nonobviousness of the claimed invention.

Applicant's arguments have been carefully considered but not found persuasive. The method claims have not been rejected under 35 USC § 103(a); and only claims 4-8, 14, and 15 are presently rejected. Therefore, in response to Applicant's argument, it is noted that the rejected claims do not require the claimed products to be used *exclusively* as recited in the claimed methods. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims and the intended or disclosed use of the invention is not given weight in comparing the claimed subject matter and subject matter disclosed by the prior art. In response to Applicant's argument that there is no proper suggestion to combine the references, the Examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, as set forth in the rejection, Dooley et al. suggests the longer duration of action resulting from the increased half-life of all D-form polypeptides makes the polypeptides more suitable for *in vivo* studies, which would have motivated one to synthesize the all D-form of the polypeptide of '926.

17. Claims 4-8, 14, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,082,926-A in view of Dooley, et al (*Science* **266**: 2019-2022, 1994) and Miles et al. (*J. Biol. Chem.* **269**: 30939-30945, 1994).

US Patent No. 5,082,926-A ('926) teaches a polypeptide having the amino acid sequence set forth in SEQ ID NO: 1. '926 teaches that the polypeptide can be conjugated or covalently bonded to a radioisotope, which is a cytotoxic agent.

However, while '926 does not teach the polypeptide must comprise all L-form amino acids, neither does '926 teach the polypeptide can comprise all D-form amino acids.

Dooley et al. teaches that polypeptides comprised of D-form amino acids are not degraded by proteases and the long duration of action resulting from the increased half-life of the all D-form polypeptide makes the polypeptides more suitable for *in vivo* studies.

Miles et al. the L- and D-enantiomers of a peptide consisting of residues 531-543 of the α1 chain fragment of the major triple helical region of type IV collagen function nearly identically, suggesting that the cell surface receptor(s) for this site do not discriminate based on chirality.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have synthesized the polypeptide of '926 in the all D-form, because Dooley et al. teaches that polypeptides in the all D-form are not degraded by proteases and are therefore expected to have longer half-lives following administration to a subject and because Miles et al. suggests the D-form peptide will function identically to the L-form peptide. One of ordinary skill in the art at the time the invention was made would have been motivated to synthesize the all D-form of the polypeptide of '926 to study the activity of the all D-form *in vivo*, because Dooley et al. suggest the longer duration of action resulting from the increased half-life of all D-form polypeptides makes the polypeptides more suitable for *in vivo* studies.

Applicant traversed the rejection of claims 4-8, 14, 15, and 32 under 35 USC § 103(a) set forth in section 16 of the previous Office action. Applicant has again argued the prior art does not teach or suggest the claimed polypeptide or conjugate thereof can be used in the claimed methods and an absence of proper motivation to combine the teachings of prior art indicates the nonobviousness of the claimed invention. Applicant's arguments have been carefully considered but not found persuasive for the reasons set forth above.

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 4-8, 14, and 15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 5,082,926-A in view of Dooley, et al (*Science* **266**: 2019-2022, 1994) for the reasons set forth in the 35 USC §103(a) rejection above.

Applicant has traversed the rejection of claims 4-8, 14, 15, and 32 for the reasons set forth in section 18 of the previous Office action arguing the rejection has been rendered moot by the amendment to the claims and in further view of the arguments traversing the rejection of the claims under 35 USC § 103(a).

Applicant's arguments have been carefully considered but not found persuasive. For the reasons set forth above in response to Applicant's arguments traversing the rejection of the claims under 35 USC § 103(a), the presently amended claims are not patentably distinct from claims 1 and 2 of U.S. Patent No. 5,082,926-A in view of Dooley, et al (*Science* **266**: 2019-2022, 1994).

20. Claims 32 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. US Patent No. 6,096,863 A.

US Patent No. 6,096,863 A teaches a peptide-conjugate comprising a polypeptide having the sequence set forth as SEQ ID NO: 1, which is in the all L-form, wherein the polypeptide is bonded to a non-peptide moiety. The non-peptide moiety of the peptide-conjugate of the prior art is an organic group having a C_6-C_{18} alkyl chain.

Conclusion

21. No claims are allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
February 25, 2004

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600